

HYPERTENSION AND CARDIOVASCULAR DISEASES ARE ONE OF THE MAIN RISKS FOR STOMATOLOGISTS PRACTICING IN RURAL COUNTIES - original study -

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Abstract

Introduction: The overall risk of dental procedures should be rigorously assessed, including the cumulative risk of latex contamination (gloves, instruments, operating fields), local anesthesia, composite materials and in addition the patient's personal risk (cardiovascular). Material and methods: the study was retrospective and was performed in a rural community, respectively Pătrăuți locality, Suceava county. Data were collected on the factors that characterize the lifestyle and working conditions of the analyzed population, heredo - collateral and personal history, anthropometric data, biochemical parameters (lipid profile, glycemia and glycated hemoglobin, BP, presence of obesity and diabetes type 2, as well as data on dental allergic risk. Results: the prevalence of hypertensive patients among the general population was 14.79% ; Adult patients diagnosed with hypertension are 34.48% male (140 patients) and 65.52% female (266 patients), the prevalence of hypertension among the adult population being 8.09% for men and 18.38% for women. Conclusions: Hypertension was a common risk factor in the study population, which raised the additional risk profile in the dental office, especially among the Roma population, decreasing the addressability to the office.

Introduction

The overall risk of dental procedures should be rigorously assessed, including the cumulative risk of latex contamination (gloves, instruments, operating fields), local anesthesia, composite materials and the patient's personal risk (cardiovascular). The dental procedures are usually performed under local anesthesia, with undergoing complications, like over dosage, toxicity, hypersensitivity and anaphylaxis. The allergic risk involves any of the maneuvers performed during an intervention in the dental medicine cabinet.

From an epidemiological point of view, essential hypertension is the main cause of cardiovascular morbidity and mortality, being known as the

"silent killer". It currently affects more than 1 billion people, or 40% of people over the age of 25, with recent reports estimating that by 2025 the number of patients will increase to 1.6 billion. Its incidence varies between 5-10% in poorly developed countries and 10-20% in industrialized ones. The global spread of the disease is also variable, being influenced by socio-economic factors and the geographical environment. Thus, the world prevalence rate is around 30 - 45%, in Romania being about 45%. Also, despite the large number of hypertensives, only 50% of them are treated. In turn, of the patients treated, more than half abandon the treatment in the first year and only 20% have controlled blood pressure values. Therefore, the

prevalence of complications such as ischemic heart disease, stroke, heart failure and cardiovascular death is also increasing [1].

The study we have conducted during 2017-2019, had several motivations, such as: increased prevalence of hypertension and cardiovascular disease, both in Romania and worldwide. Cardiovascular diseases remain the leading

cause of cardiovascular morbidity and mortality in most developed countries, they are a major public health problem (one of the most common reasons for outpatient medical consultation, leads to the prescription of an increased number of drugs). High blood pressure is a major risk factor in the development of atherosclerosis in the brain, coronary and renal (Table I).

Table I: Pathological values of blood pressure by age (according to Gherasim et al., 2000)

Age	TAS (mmHg)	TAD (mmHg)
3 - 5 years	> 116	> 76
6 - 9 years	> 122	> 78
10 - 12 years	> 126	> 82
13 - 15 years	> 136	> 86
Over 16 years	> 140	> 90

Despite the progress made in recent years in understanding this disease, the rate of control of blood pressure has remained low, although several classes of drugs with antihypertensive effect are known, and new therapeutic options, in most cases, are not accessible to patients from disadvantaged social environments, for economic reasons.

An extremely important part in defining the disease is the clinical and paraclinical evaluation of the hypertensive patient. This involves

general elements and particular elements for each patient, the objectives of the evaluation being to establish the basic characteristics of hypertension (values, variations), identification of target organ damage (brain, heart, kidneys, fundus), evaluation of existing cardiovascular risk factors and identification comorbidities [2,3].

Essential hypertension is a condition characterized by multiple changes in the vascular level, including endothelial

dysfunction, exacerbation of vasoconstrictor effects, vascular remodeling, inflammation, fibrosis and increased stiffness of the arteries [4].

However, despite the high incidence, essential

hypertension(HBP) has no known etiology. However, a number of etiological factors of the disease are known (Table II).

Table II. Etiopathogeny of hypertension risk factors (dupa Căpâlneanu, 2014) [5]

<p>Heredity is considered a first etiological factor, epidemiological studies performed on families of hypertensives showing that this factor contributes to the occurrence of hypertension in 30-60% of cases, even if parents and the descendants live in different environmental conditions.</p>
<p>Sex is not a determining factor in blood pressure, but in postmenopausal women there is a lower incidence and severity of hypertension. The incidence is relatively balanced between the two sexes up to the age of 60, after which it increases in women.</p>
<p>The age of the patients is important, as after 60 years there is an increase in blood pressure values by about 5-10 mmHg / year due, in particular, to the reduction of vessel elasticity.</p>
<p>Race can also influence the onset of the disease, with the incidence of hypertension being higher in the black adult population compared to the Caucasian race.</p>
<p>Dietary salt intake is the most important etiological factor in the occurrence of essential hypertension. The pathogenic role of sodium has been demonstrated by epidemiological studies performed on populations consuming excess salt. However, the relationship between increased salt intake and the occurrence of the disease must be correlated with the existence of genetic defects with a role in the transmembrane transport of sodium.</p>
<p>An increased dietary intake of calcium, potassium and / or magnesium appears to have a protective role against the increase in BP.</p>
<p>Obesity is also an important etiological factor, with numerous studies showing that high blood pressure is more common in obese people, the most vulnerable being obese children and adolescents.</p>

Alcohol consumption leads to increased blood pressure, especially when there are other associated risk factors.

Smoking causes short-term increases in blood pressure and increases the risk of cardiovascular and cerebral complications of hypertension, as well as the risk of progression to malignant hypertension.

Caffeine consumption causes acute increases in BP, but patients frequently develop a caffeine tolerance effect.

Sedentary lifestyle increases the risk of hypertension, especially when there are other associated risk factors.

Psycho-emotional factors play a role in determining hypertension.

The association of some comorbidities (for example, diabetes or atherosclerosis) can lead to a 2-3-fold increase in the risk of hypertension [6,7].

The initial clinical evaluation begins with the anamnesis, respectively with the establishment of the signs and symptoms of the patient and their conditions of appearance. High blood pressure is frequently asymptomatic, being discovered by chance [7], but some patients may have headaches (often occipital, throbbing or constrictive), excessive sweating, facial erythema or even palpitations, agitation and insomnia [8]. In complicated forms, patients show symptoms and signs specific to target organ damage (eg, angina pectoris, dyspnea)[7].

Identifying the hereditary - collateral antecedents of hypertension and other cardiovascular diseases with the specification of their evolution is important, as many of them have a significant hereditary component. It is also necessary to establish a personal pathological history to identify other pathologies

that may influence the evolution and treatment of hypertension (ischemic, lung, kidney)[8].

Establishing living and working conditions aims to identify cardiovascular risk factors, such as smoking, alcohol consumption, excessive salt consumption, coffee, the presence of stress or exposure to various toxic substances. In addition, information on treatments for hypertension or other diseases should be included, as well as data such as type of medication, doses administered, duration of treatment and patient compliance [9, 10].

Cardiovascular risk factors are those factors that influence the evolution of the disease at 10 years to major cardiovascular events. The totality of the factors present in a patient constitutes the global cardiovascular risk, and its evaluation includes both the risk factors themselves and the evaluation of the damage to the target organs [11].

The main purpose of this retrospective study was to analyze hypertension treatment

methods in adults from a rural community in NE Romania.

The main objectives were the following:

1. Gathering information on the prevalence of hypertension in the respective rural community, correlated with cardiovascular risk factors
2. Highlighting the particularities of therapeutic approach in that community
3. Using the results obtained to assess the impact on risk factors

Material and methods

In the study, data were collected on the factors that characterize the lifestyle and working conditions of the analyzed population, heredo-collateral and personal history, anthropometric data, biochemical parameters(lipid profile, glycemia and glycated hemoglobin, BP, presence of obesity and diabetes type 2, as well as data on the treatment followed.

Study population and data collection: the study was retrospective and was performed in a rural community, respectively Pătrăuți locality, Suceava county. This locality was chosen due to its population, level of education and ethnic, cultural and religious uniformity. Population data were collected with the help of one of the local family doctors, based on information from medical records. Excluded from this group of patients were those under 18 years of age, those who refused to participate in the study, patients with secondary hypertension, and patients with psychiatric disorders, who were completely excluded from the final analysis. The rural community in which the study was conducted has, according to the last census, a total population of 4567 inhabitants, with an

approximately equal sex ratio of 2262 (49.52%) men and 2305 (50.47%) women. The population has an unique feature, being composed by almost 50% gipsy people, establish in the area from the beginning of last century.

Statistical Data: the results of the study were obtained using the descriptive functions of the statistical analysis program SPSS v 25.0. The tests for evaluating the homogeneous distribution of the Skewness / Kurtosis continuous variables were used, a result of which in the range [-2, 2] revealing a homogeneous distribution. Assessment of statistical percentage differences were performed using tests such as the t-student test, parametric test applied to continuous variables, normal distribution, to differentiate between two groups at a threshold of statistical significance of 95%. The Mann-Whitney U test is a non-parametric test used for the same purpose as the t-student test, but applied to variables with inhomogeneous distribution. The statistical correlation Kendall-tau b test is a test applied to continuous/ordinal variables to determine if there is a correlation between them.

In terms of age distribution, the population can be divided into : people under 18 - 1390 (30.43%); people between 18 and 65 - 2344 (51.32% of the population), of which 1203 (26.34%) men and 1141 (24.98%) women and people over 65 years - 833 (18.23%), of whom 527 (11.53%) men and 306 (6.7%) women. In the records of the collaborating family doctor there are a total of 2745 people, of which 1310 (47.72%) men and 1435 (52, 28%) women, with the following distribution by age: people under the age of 18 - 794 (28.9%); people aged between 18 and 65 - 1635 (59.6%), of which 716 (43.8%) men and 919 (56.2%) women; people aged 65 to 90 - 309 (11.2%), of whom 114

(36.9%) men and 195 (63.1%) women; people over 90 years - 7 (0.2%), of which one man (14.28%) and 6 women (85.72%).

Patients chosen for the final analysis are those of adult age (over 18 years) who met the diagnostic criteria for hypertension according to the ESC / ESH Guide for the management of hypertension 2018 (systolic BP \geq 140 mmHg or diastolic BP \geq 90 mmHg) and those previously diagnosed with essential hypertension. The diagnosis of hypertension was confirmed after the determination of BP both in a sitting position and in an orthostatic position, after a 5-minute rest of the patients. 3 measurements were performed for each patient, with rest periods of 1-2 minutes between measurements and an average of the 3 detected values was recorded, establishing, at the same time, the severity of the disease.

After establishing the group of patients according to the diagnosis of essential hypertension, data were collected on the treatment of each patient, as well as data on the presence of cardiovascular risk factors (smoking, stress, the presence of hereditary factors, blood biochemical parameters), comorbidities and complications specific to hypertension.

Treatment data followed by patients were taken from medical records. These were then sorted

according to the classes of drugs to which the prescribed active substances belong, as well as according to the classification of these classes in the category of antihypertensive drugs.

Results

For the final analysis, following the selection criteria described above, a study group of 406 patients aged between 26 and 96 years was performed.

After establishing the group of patients, it was determined that the prevalence of hypertensive patients among the general population was 14.79%. Adult patients diagnosed with hypertension are 34.48% male (140 patients) and 65.52% female (266 patients), the prevalence of hypertension among the adult population being 8.09% for men and 18.38% for women.

The patients included in the group had a mean age of 62.39 ± 12.31 years, with variations between 26 and 96 years, and a median group of 62 years. The mean value was close to the median value, and the results of the Skewness ($p = -0.014$) and Kurtosis ($p = -0.613$) tests located in the range $[-2, 2]$ show a homogeneous distribution of values. Female hypertensive patients were older compared to male patients, the difference between the sexes (3.17 years) being statistically significant ($p = 0.008$) (Table III)

Table nr. III. Descriptors of patients distribution by age and gender

Gender	N	Average	Deviation Std.	Std error.	Confidence interval 95%		Min	Max	p
					-95% CI	+ 95% CI			
Male	140	60.31	11.89	1.01	58.32	62.29	31	96	
Female	266	63.48	12.04	0.76	61.99	64.98	26	92	0.008
Total	406	62.39	12.31	0.61	61.19	63.59	26	96	

The majority of patients in the group were female (266 cases, 65.5%), the ratio of females: males being 1.85: 1. In addition to the presence of hypertension, some patients in the group also had other important cardiovascular risk factors, which may influence the choice of antihypertensive treatment, such as smoking, obesity and diabetes(**Table nr. IV**). Thus,

although most hypertensive patients reported non-smoking (350 patients, 86.2%), a relatively small number of smokers (30 cases, 7.6%) and former smokers were identified (26 cases, 6.4%). It was also found that the majority of smokers were men (26 cases, representing 86.6% of smokers)(**Table nr. V**)

Table nr. IV. Main Mean deviations for the study group regarding age, gender, biochemical data and risk factors(obesity, diabetes and HBP)

		Statistics ^a										
		Age	Gender	Obesity	Diabetes type 2	Hereditary	Tryglicerides	LDL	Uric acid	HbA1c	HBP	CCS
N	Valid	149	155	154	155	155	113	39	155	19	155	155
	Missing	6	0	1	0	0	42	116	0	136	0	0

Mean	57,48	1,58	2,27	1,15	1,73	160,03	124,55	7,5225	8,11	1,97	1,39
Median	54,00	2,00	2,00	1,00	1,00	137,00	120,00	7,1000	8,01	2,00	1,00
Mode	53	2	1	1	1	77 ^b	120	6,30	6	2	1
Std. Deviation	11,962	,495	1,216	,357	1,089	88,658	32,602	1,12809	2,298	,738	,489

a. Ethnicity = Gypsy ethnicity

b. Multiple modes exist. The smallest value is shown

Table nr. V. Distribution of patients after the main descriptors: age, gender, metabolic profile, obesity, diabetes, HBP and CCS

Ethnicity		Statistics										
		Age	Gender	Obesity	Diabetes type 2	Hereditary	Tryglicerides	LDL	Uric acid	HbA1c	HBP	CCS
Gypsy ethnicity	N	149	155	154	155	155	113	39	155	19	155	155
	Valid											
	Missing	6	0	1	0	0	42	116	0	136	0	0
	Mean	57,48	1,58	2,27	1,15	1,73	160,03	124,55	7,5225	8,11	1,97	1,39
	Median	54,00	2,00	2,00	1,00	1,00	137,00	120,00	7,1000	8,01	2,00	1,00
	Mode	53	2	1	1	1	77 ^a	120	6,30	6	2	1
Caucasian	N	251	251	251	251	250	199	61	251	20	251	251
	Valid											
	Missing	0	0	0	0	1	52	190	0	231	0	0
	Mean	65,16	1,70	1,74	1,13	1,46	150,49	123,00	4,5298	7,81	1,75	1,55
	Median	65,00	2,00	1,00	1,00	1,00	115,00	119,30	4,9000	7,45	2,00	2,00
	Mode	62	2	1	1	1	104	112 ^a	5,50	6 ^a	1	2
Gypsy ethnicity	N	149	155	154	155	155	113	39	155	19	155	155
	Valid											
	Missing	6	0	1	0	0	42	116	0	136	0	0
	Mean	57,48	1,58	2,27	1,15	1,73	160,03	124,55	7,5225	8,11	1,97	1,39
	Median	54,00	2,00	2,00	1,00	1,00	137,00	120,00	7,1000	8,01	2,00	1,00
	Mode	53	2	1	1	1	77 ^a	120	6,30	6	2	1
Caucasian	N	251	251	251	251	250	199	61	251	20	251	251
	Valid											
	Missing	0	0	0	0	1	52	190	0	231	0	0
	Mean	65,16	1,70	1,74	1,13	1,46	150,49	123,00	4,5298	7,81	1,75	1,55
	Median	65,00	2,00	1,00	1,00	1,00	115,00	119,30	4,9000	7,45	2,00	2,00
	Mode	62	2	1	1	1	104	112 ^a	5,50	6 ^a	1	2
Gypsy ethnicity	N	149	155	154	155	155	113	39	155	19	155	155
	Valid											
	Missing	6	0	1	0	0	42	116	0	136	0	0
	Mean	57,48	1,58	2,27	1,15	1,73	160,03	124,55	7,5225	8,11	1,97	1,39
	Median	54,00	2,00	2,00	1,00	1,00	137,00	120,00	7,1000	8,01	2,00	1,00
	Mode	53	2	1	1	1	77 ^a	120	6,30	6	2	1
Caucasian	N	251	251	251	251	250	199	61	251	20	251	251
	Valid											
	Missing	0	0	0	0	1	52	190	0	231	0	0
	Mean	65,16	1,70	1,74	1,13	1,46	150,49	123,00	4,5298	7,81	1,75	1,55
	Median	65,00	2,00	1,00	1,00	1,00	115,00	119,30	4,9000	7,45	2,00	2,00
	Mode	62	2	1	1	1	104	112 ^a	5,50	6 ^a	1	2

a. Multiple modes exist. The smallest value is shown

In the group of patients investigated, there were no significant differences in terms of smoking between Caucasian patients and Roma patients (**Table nr. VI**).

Table nr. VI. Variances upon ethnic smoking distribution

		Independent Samples Test								
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Smoking	Equal variances assumed	1,122	,290	-,411	403	,681	-,036	,087	-,208	,136
	Equal variances not assumed			-,424	355,659	,672	-,036	,085	-,203	,131

We have observed that, for the studied population, obesity, hypertension and heredity **significantly influence** the health status of the

Roma population compared to the Caucasian population, but CCS occurs more frequently in the Caucasian population (Table nr. VII)

Table nr. VII. Variances of main diseases linked to ethnicity and hereditary inheritance

		Independent Samples Test								
		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Obesity	Equal variances assumed	19,370	,000	4,690	403	,000	,525	,112	,305	,745

	Equal variances not assumed			4,491	279,879	,000	,525	,117	,295	,755
Diabetes type 2	Equal variances assumed	1,408	,236	,597	404	,551	,021	,035	-,048	,090
	Equal variances not assumed			,587	310,120	,557	,021	,036	-,049	,091
HbA1c	Equal variances assumed	,646	,427	,446	37	,658	,303	,679	-1,072	1,678
	Equal variances not assumed			,444	35,248	,660	,303	,682	-1,081	1,686
HBP	Equal variances assumed	4,668	,031	2,980	404	,003	,225	,076	,077	,374
	Equal variances not assumed			2,982	327,187	,003	,225	,076	,077	,374
CCS	Equal variances assumed	6,552	,011	-3,219	404	,001	-,163	,051	-,262	-,063
	Equal variances not assumed			-3,234	331,264	,001	-,163	,050	-,262	-,064
Stress	Equal variances assumed	,012	,913	-,054	404	,957	-,003	,048	-,096	,091
	Equal variances not assumed			-,054	326,517	,957	-,003	,048	-,096	,091

Heredit y	Equal variances assumed	6,027	,015	2,54	403	,011	,269	,106	,061	,477
	Equal variances not assumed			5						
				2,49	305,	,013	,269	,108	,057	,481
				4	045					

Predictive model Diabetes type II comparison Caucasians-Roma (Figure nr.1) shows that, in a percentage of 28.2%, the variable type II diabetes is predicted by uric acid, HDL, heredity,

gender, CCS, obesity, LDL, followed by tryglicerides, forthe Caucasian population in the investigated group (Table nr VIII), (Fig nr. 1).

Table nr VIII. Postive regression for Gipsy/Roma versus Caucasians by Uric Acid

		ANOVA ^a						
				Sum of	df	Mean Square	F	Sig.
Ethnicity	Model			Squares				
Gypsy ethnicity	1	Regression		1,797	8	,225	1,536	,193 ^b
		Residual		3,803	26	,146		
		Total		5,600	34			
Caucasian	1	Regression		2,601	8	,325	2,109	,050 ^c
		Residual		6,629	43	,154		
		Total		9,231	51			

a. Dependent Variable: Diabetes type 2

b. Predictors: (Constant), Uric acid, Heredity, HDL, CCS, LDL, Tryglicerides, Obesity, Gender

c. Predictors: (Constant), Uric acid, HDL, Heredity, Gender, CCS, Obesity, LDL, Tryglicerides

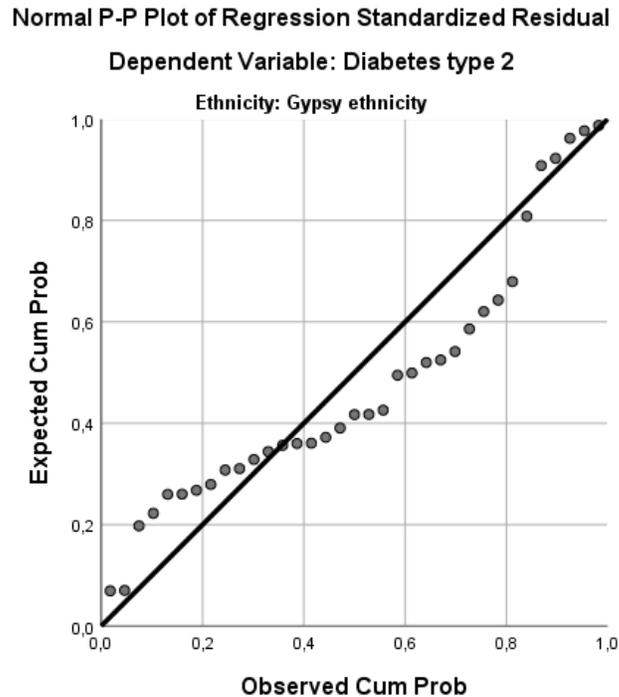


Figure nr.1. Positive Regression Curve for Diabetes in Roma and Caucasians

Discussions

Following the study, it could be determined that the prevalence of hypertensive patients among the general population in the chosen community was lower than the prevalence of the disease at national and European level, respectively. Thus, the prevalence was 14.79%, compared to the estimated global prevalence between 30% and 45% [11]. This is most likely due to an increased rate of underdiagnosis generated by the low percentage of patients who go to the doctor for a consultation.

Of the 406 patients included in the study, the majority were female (65.52%). In addition, female patients were older compared to male patients, the difference between the sexes (3.17 years) being statistically significant ($p = 0.008$).

Also, most patients had blood pressure values corresponding to grade 2 hypertension (170 cases, 41.9%).

In addition to hypertension, other major cardiovascular risk factors were identified in the selected patients, such as smoking, obesity and diabetes. However, none of these factors were present in a significant proportion in the study population, the majority of patients being, declaratively, non-smokers (86.2%), normal weight (51.2%) and non-diabetics (85.7 %).

Of the patients chosen in our study, only 91.9% follow an antihypertensive treatment with at least one drug from the recommended hypertensive classes, among the reasons for refusing the drug treatment are low incomes, low level of education or social environment,

compliance rates being low in rural areas, as stated in other studies [10, 12].

Conclusions

The prevalence of hypertension in the studied community was 18.38% in women and 8.09% in men. High blood pressure was also more common in patients between the ages of 40 and 64 and with a combination of cardiovascular risk factors.

Treatment of hypertension in the rural community studied, though followed the guidelines, sometimes required their adaptation to the particularities of the population, being influenced mainly by the socioeconomic level of patients and implicitly by the existence of an overwhelming proportion of Roma population, with low compliance with prevention methods applied early.

The involvement of social and economic factors in the acceptance of certain treatments is noticeable, preferring the use of generic drugs and cheaper classes. Fixed combinations were also not approved, most often due to the high cost.

The percentage of patients undergoing antihypertensive treatment and compliance with treatment increased with increasing severity of the disease, treatment compliance being better among women and elderly patients, who strictly followed the hygienic diet.

Hypertension was a common risk factor in the study population, which raised the additional risk profile in the dental office, especially among the Roma population, decreasing the addressability to the office.

All authors have equally contributed.

References

1. Costache I. I., Miftode E., Mitu O., Costache A. D., Aursulesei V. Arterial Hypertension Prevalence in a Romanian Rural Community: Correlations with Social and Economic Status, Age and Gender. *Revista de cercetare și intervenție socială* 2017; 59:62-74.
2. Costache Irina Iuliana, Cozma Alexandru., Aursulesei Viviana. Hipertensiunea arterială secundară. În: Aursulesei V., Bădilă E., Bartoș D. (sub redacția), HTA de la practică la teorie, de la pacienți la ghiduri. Editura Niculescu, București, 2017, 209-230
3. Costache II, Miftode E, Mitu O, Aursulesei V, Sex Differences in Cardiovascular Risk Factors in a Rural Community from North Romania Region, *Revista de Cercetare si Interventie Sociala* 55 , pp.204-214, dec 2016
4. Cameron, A. C., Lang, N. N., & Touyz, R. M. Drug Treatment of Hypertension: Focus on Vascular Health. *Drugs*, 2016, 76(16), 1529–1550.
5. Williams B., Mancia G. și colab. 2018 ESC/ESH Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *European Heart Journal* 2018; 39:3021-3104
6. Hering D., Trzebski A., Narkiewicz K. Recent advances in the pathophysiology of arterial hypertension: potential implications for clinical practice. *Polish Archives Of Internal Medicine*, 2017; 127 (3)
7. Imprialos K. P., Boutari C., Stavropoulos K., Doumas M., Athyros V. G., Karagiannis A. I. Current challenges in antihypertensive treatment in the elderly. *Polish Archives Of Internal Medicine* 2016; 126 (7-8).
8. Kjeldsen S. E., Stenehjem A., Os I., Van de Borne P., Burnier M., Narkiewicz K., Redon J., Rosei E. A. & Mancia G. Treatment of high blood pressure in elderly and octogenarians: European Society of Hypertension statement on blood pressure targets. *Blood Pressure*, 2016, 25:6, 333-336

9. Namat et al, heart-type fatty acid-binding protein (h-fabp) in patients with coronary artery bypass graft surgery undergoing cardiac rehabilitation program, *Revista de chimie* 68 (7) , pp.1485-1489, July 2017
10. Wang, A. L., Iadecola, C., & Wang, G. New generations of dihydropyridines for treatment of hypertension. *Journal of geriatric cardiology : JGC*, 2017, 14(1), 67–72.
11. Williams B., Mancia G. și colab. 2018 ESC/ESH Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *European Heart Journal* 2018; 39:3021-3104
12. Williams, B., MacDonald, T. M., Morant, S., Webb, D. J., Sever, P., McInnes, G. și colab. Spironolactone versus placebo, bisoprolol, and doxazosin to determine the optimal treatment for drug-resistant hypertension (PATHWAY-2): a randomised, double-blind, crossover trial. *The Lancet*, 2015, 386(10008), 2059–2068.